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Stereodynamics of 2-Alkoxy-3-halobutanes and 2-Acetoxy-3-halobutanes. Experimental DNMR Studies and Theoretical Investigations of Carbon–Carbon Single Bond Rotation, Rotamer Preferences, and Solvent Effects

Chih Y. Wang and C. Hackett Bushweller*[1]

Contribution from the Department of Chemistry, Worcester Polytechnic Institute, Worcester, Massachusetts 01609. *Received April 1, 1976*

Abstract: Examination of the ^1H DNMR spectra of a series of 2-alkoxy-3-halo-2,3-dimethylbutanes, 2-acetoxy-3-halo-2,3-dimethylbutanes, and 2,2-dialkoxy-3,3-dihalobutanes shows changes consistent with slowing rotation about the C(2)–C(3) bond and the presence of gauche and trans rotamers. For all of the compounds in either vinyl chloride or bromotrifluoromethane as solvent, the gauche rotamer is observed to be at lower enthalpy than the trans but the trans is observed to be at higher entropy than the gauche. Indeed, in all cases, it is then the trans rotamer which is favored by free energy indicating that entropy plays an important role in determining conformational preference in these systems most likely as a result of differential dipolar solvation. Theoretical ^1H DNMR line shape analyses of the exchange-broadened spectra are consistent with a dynamical model incorporating lower barriers for the gauche to trans to gauche equilibration than for the direct gauche to gauche process.

In attempting to rationalize trends in conformational preference and potential barriers for rotation about carbon–carbon single bonds, both steric and electrostatic factors need to be considered.[2] For some molecular systems having two vicinal electronegative substituents bonded to adjacent sp^3-hybridized carbon atoms, it is evident from available data that placing two highly electronegative groups in close proximity does not necessarily lead to a situation dominated by repulsive dipolar interactions.[3] For example, in the case of gaseous 1,2-difluoroethane, the gauche rotamer is favored by about 0.6 kcal/mol over the trans[4] in spite of a more parallel alignment of the two C–F bond moments and the close proximity of the two fluorine atoms. Rationales have been presented to account for such interesting conformational preferences including the "gauche effect" which in essence invokes a dominant electron-nuclear attraction between the two proximate gauche fluorines.[5] Other approaches are based on orbital-control mechanisms[6] and force-field calculations.[7]

In proceeding from the gaseous to the liquid state for the 1,2-dihaloethanes, there is a significant *increase* in the amount of gauche forms due most likely to a lowering of the enthalpy of the polar gauche rotamer via dipole–dipole solvation.[2,8-10]

For more complex systems which are homologous or analogous to the dihaloethanes discussed above, the ^1H DNMR method provides a powerful tool for study of gauche vs. trans preference as well as rates of rotation about the central carbon–carbon bond *if* the potential barrier for rotation is in the range of 5–20 kcal/mol.[11] In spite of the obvious utility of the DNMR method for the study of such moderately hindered systems, relatively few reports have been forthcoming regarding DNMR investigations of the stereodynamics of more complex 1,2-dihaloethane homologues and related systems.[3,12]

This report concerns solution ^1H DNMR investigations of a series of 2-alkoxy-3-halo-2,3-dimethylbutanes, 2-acetoxy-3-halo-2,3-dimethylbutanes, and 2,2-dialkoxy-3,3-dihalobutanes which allow the determination of both conformational preference and potential barriers to rotation about the central C(2)–C(3) bond.

Results

Examination of the ^1H DNMR spectrum (60 MHz) of 2-bromo-3-methoxy-2,3-dimethylbutane (**1**; 3% v/v in CH_2CHCl) at −39.8 °C shows three singlet resonances at δ 1.34 (6 H, $OC(CH_3)_2$; Figure 1), 1.76 (6 H, $BrC(CH_3)_2$), and 3.20 (3 H, OCH_3) consistent with rapid rotation about the C(2)–C(3) bond on the DNMR time scale. The chemical shift assignments for the gem-dimethyl resonances in **1** were made after consideration of chemical shift trends in all the compounds of interest in this work and in a previously studied series of 2-halo-2,3,3-trimethylbutanes[12] and in 2-methoxy-2,3,3-trimethylbutane.[13]

At temperatures below −70 °C, the $OC(CH_3)_3$ resonance broadens asymmetrically (Figure 1) and then sharpens at −110.5 °C into two small singlets of *equal area* at δ 1.12 and

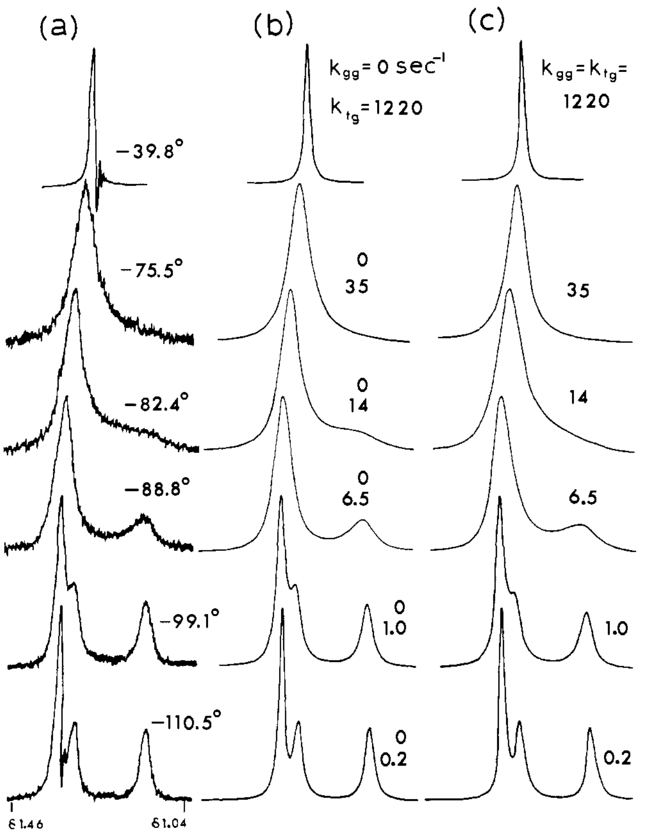
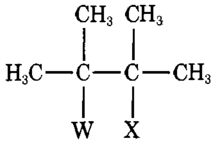
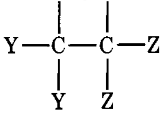


Figure 1. (a) Experimental ^1H DNMR spectra (60 MHz) of the $OC(CH_3)_2$ resonance of 2-bromo-3-methoxy-2,3-dimethylbutane (**1**; 5% v/v in CH_2CHCl) at various temperatures. (b) Theoretical ^1H DNMR spectra calculated as a function of the rate of trans/gauche equilibration assuming *no* gauche to gauche exchange (k_{gg} and k_{tg} are respectively the first-order rate constants for the gauche to gauche and trans to gauche processes). (c) Theoretical ^1H DNMR spectra calculated using *equal* rate constants for the gauche to gauche to trans to gauche processes.



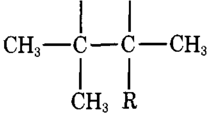
$$\begin{array}{ccccccc} & & CH_3 & & CH_3 & & \\ & & | & & | & & \\ H_3C & — & C & — & C & — & CH_3 \\ & & | & & | & & \\ & & W & & X & & \end{array}$$

1, W = Br; X = OCH_3
2, W = Cl; X = OCH_3
3, W = Br; X = OCH_2CH_3
4, W = Cl; X = OCH_2CH_3
5, W = Br; X = O_2CCH_3
6, W = Cl; X = O_2CCH_3



$$\begin{array}{ccccc} & CH_3 & & CH_3 & \\ & | & & | & \\ Y & — C — & & C — & Z \\ & | & & | & \\ & Y & & Z & \end{array}$$

7, Y = Br; Z = OCH_3
8, Y = Cl; Z = OCH_3
9, Y = Br; Z = OCH_2CH_3
10, Y = Cl; Z = OCH_2CH_3

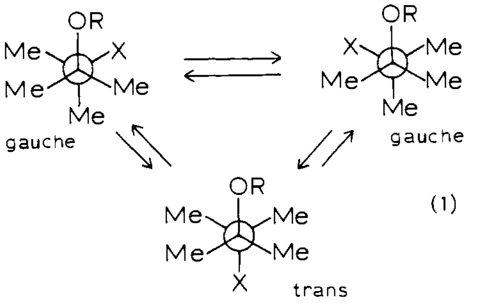


$$\begin{array}{ccccccc} & & CH_3 & & OCH_3 & & \\ & & | & & | & & \\ CH_3 & — & C & — & C & — & CH_3 \\ & & | & & | & & \\ & & CH_3 & & R & & \end{array}$$

11, R = OCH_3
12, R = CH_3

1.34 and a larger singlet at δ 1.38. The ratio of the total area under both small singlets to the area under the large singlet is 57:43 at −110 °C. The $BrC(CH_3)_2$ and OCH_3 resonances are not split into separate resonances at −110 °C although they are broader than at −39.8 °C. Examination of the ^1H DNMR spectrum of **1** as a 5% v/v solution in $CBrF_3$ at −68 °C shows an $OC(CH_3)_2$ singlet (δ 1.40) which is separated at −110 °C into two small singlets of *equal area* at δ 1.17 and 1.40 and a larger singlet at δ 1.43. The ratio of the total area under the two small singlets to the area under the large singlet is now 38:62 at −110 °C. In addition, the OCH_3 resonance (δ 3.25 at −68 °C) broadens asymmetrically and is separated at −110 °C into two singlets at δ 3.28 and 3.24 with a respective area ratio of 38:62. The $BrC(CH_3)_2$ resonance is not separated into distinct resonances at −110 °C.

Such DNMR spectral behavior is completely consistent with slowing rotation about the central C(2)–C(3) bond of **1** and slow gauche to trans equilibration (eq 1, R = CH_3; X = Br).



(1)

The observation of *singlet* methyl resonances at −110 °C is also consistent with individual methyl group rotation being fast on the DNMR time scale at this temperature.[14] For the $OC(CH_3)_2$ resonance at −110 °C (Figure 1), the two small singlets of equal area may be assigned to the two nonequivalent methyl groups of either of the two enantiomeric gauche rotamers (eq 1) and the larger singlet to the two equivalent methyl groups of the trans (eq 1). Such assignments are unequivocal and allow a direct determination of the equilibrium constant between gauche and trans rotamers at different temperatures. It is apparent from the peak area ratios cited earlier in CH_2CHCl and $CBrF_3$ that the gauche:trans ratio is solvent dependent.

Thus, we performed careful measurements of the gauche to trans ratio in **1** as a function of temperature using *complete DNMR line shape analysis*[15] to measure peak areas and employing radiofrequency power levels well below saturation. The error in temperature measurement at the sample is ±0.2 °C (see Experimental Section). Use of the complete line shape method to determine the equilibrium constants resulted in excellent precision (±2%) for a given equilibrium constant measured from several different spectra at a given temperature. This approach is clearly preferable to electronic integration, hand planimetry, or weighing peak cutouts which all give a precision of about ±8%. For both solvent systems (CH_2CHCl and $CBrF_3$), van't Hoff plots of ln K_{eq} vs. $1/T$ gave the $\Delta H°$, $\Delta S°$, and $\Delta G°$ values compiled in Table I. In Table I, the thermodynamic parameters have been corrected for the statistical preference of two for the two enantiomeric gauche rotamers.

At temperatures above −110 °C, the shape of the ^1H DNMR spectrum of the $OC(CH_3)_2$ group of **1** is a a function of the rate of C(2)–C(3) rotation (eq 1; Figure 1). The observation of *two* methyl singlets for the gauche and a separate larger singlet for the trans at −110 °C reveals both the gauche to trans and gauche to gauche equilibrations to be slow on the DNMR time scale. At higher temperatures, all of these signals average to a single resonance. In a qualitative sense, there are two dynamical models which could account for such spectral behavior: (1) the barriers for the trans to gauche, gauche to trans, and gauche to gauche equilibrations are all comparable, (2) the barriers for the gauche to trans to gauche equilibration are significantly smaller than that for the gauche to gauche process. These two cases and indeed an infinite number of intermediate situations allow complete site exchange of the

Table I. Thermodynamic Parameters[a] for Gauche to Trans Equilibration

Compd	Solvent (% solute, v/v)	$\Delta H°$, kcal/mol	$\Delta S°$, gibbs	$\Delta G°$ (−110 °C), kcal/mol
1	CH_2CHCl (3)	0.89 ± 0.06	6.3 ± 0.1	−0.14 ± 0.02
	$CBrF_3$ (5)	0.50 ± 0.04	5.0 ± 0.2	−0.38 ± 0.02
2	CH_2CHCl (3)	0.52 ± 0.05	5.4 ± 0.2	−0.36 ± 0.02
	$CBrF_3$ (5)	0.24 ± 0.05	4.6 ± 0.2	−0.50 ± 0.02
3	CH_2CHCl (5)			−0.34 ± 0.04
4	CH_2CHCl (5)			−0.56 ± 0.04
5	CH_2CHCl (5)	0.75 ± 0.03	5.2 ± 0.4	−0.10 ± 0.02
6	CH_2CHCl (5)	0.72 ± 0.04	5.9 ± 0.4	−0.24 ± 0.02
7	$CBrF_3$ (5)	0.49 ± 0.04	5.5 ± 0.3	−0.41 ± 0.02
8	$CBrF_3$ (5)	0.42 ± 0.05	4.6 ± 0.2	−0.33 ± 0.02
9	CH_2CHCl (5)	0.40 ± 0.02	5.3 ± 0.4	−0.47 ± 0.02
10	CH_2CHCl (5)	0.30 ± 0.10	4.3 ± 0.6	−0.40 ± 0.04

[a] Corrected for statistical preference for gauche; K_{eq} = [trans]/[gauche].

Table II. ^1H DNMR Chemical Shifts of Pertinent Resonances under Conditions of Slow C(2)–C(3) Rotation

Compd	Dynamic resonance	^1H chemical shifts, ppm	
		Trans	Gauche
1	$OC(CH_3)_2$	1.38[a]	1.34, 1.12[a]
		1.43[b]	1.40, 1.17[b]
2	$OC(CH_3)_2$	1.32[a]	1.30, 1.13[a]
		1.29[b]	1.29, 1.12[b]
3[a]	$OC(CH_3)_2$	1.39	1.35, 1.12
	$CH_3(Et)$	1.08 (^3J = 7.0 Hz)	1.13 (^3J = 7.0 Hz)
4[a]	$OC(CH_3)_2$	1.31	1.29, 1.14
	$CH_3(Et)$	1.10 (^3J = 6.8 Hz)	1.14 (^3J = 6.8 Hz)
5[a]	$OC(CH_3)_2$	1.74	1.74, 1.51
	$BrC(CH_3)_2$	1.80	1.83, 1.74
	O_2CCH_3	1.94	1.98
6[a,c]	$OC(CH_3)_2$	1.68	1.68, 1.54
	$ClC(CH_3)_2$	1.61	1.64, 1.53
	O_2CCH_3	1.95	1.98
7[b]	$OCCH_3$	1.88	1.51
	$BrCCH_3$	2.50	2.47
	OCH_3	3.44	3.47, 3.38
8[b]	$OCCH_3$	1.73	1.46
	$ClCCH_3$	2.09	2.07
	OCH_3	3.39	3.39, 3.32
9[a]	$OCCH_3$	1.87	1.53
	$BrCCH_3$	2.52	2.45
10[a]	$OCCH_3$	1.75	1.50
	$ClCCH_3$	2.11	2.08

[a] Solvent: CH_2CHCl. [b] Solvent: $CBrF_3$. [c] Due to close proximity of $OC(CH_3)_2$ and $ClC(CH_3)_2$ resonances, the chemical shift assignments listed here are tentative.

$OC(CH_3)_2$ methyl groups in **1**. For the same *net* conformational exchange (e.g., gauche to gauche equilibration) which may occur by different itineraries (e.g., a *direct* gauche to gauche process *or* a gauche to trans to gauche route), the shape of the exchange-broadened DNMR spectra will be most sensitive to the lowest barrier itinerary. In fact, the DNMR model[15] used to obtain an excellent fit of experimental to theoretical spectra (Figure 1b) incorporated an effective rate constant of zero for the gauche to gauche process over the temperature range from −39.8 to −110.5 °C (Figure 1) and variable rates of gauche to trans equilibration. Variations in the gauche to trans ratio in the various exchange-broadened DNMR spectra of Figure 1 were obtained from an extrapolation of such trends established from the measurement of K_{eq} at lower temperatures discussed above (Table I). Indeed, some of the significantly exchange-broadened spectra (e.g., at −82.4 and −88.8 °C) were quite sensitive to changes in rotamer populations and the independently determined values necessary for a good spectral fit were completely consistent with an extrapolation of those obtained at slow exchange temperatures.

The use of a rate constant of zero for the gauche to gauche process in **1** does not of course imply that this rate is actually zero but only that the process occurs at a significantly slower rate on the DNMR time scale than the gauche to trans to gauche equilibrations. Indeed, generation of theoretical DNMR line shapes using other dynamical models indicates that the barrier for the gauche to gauche equilibration is at least 0.5 kcal/mol higher than that for the trans to gauche or gauche to trans processes. Illustrated in Figure 1c are theoretical spectra calculated using *equal* rate constants for the gauche to gauche and trans to gauche processes. It is evident that these spectra do not give an acceptable fit to the experimental.

Compiled in Table II are the slow-rotation ^1H chemical shift values for the $OC(CH_3)_2$ resonances of the gauche and trans forms of **1** as well as pertinent resonances for all of the other compounds discussed in this paper.

Table III. Activation Parameters for Pertinent Rate Processes

Compd	Rate process	Solvent	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, gibbs	$\Delta G^{\ddagger}$, kcal/mol (T, °C)
1	tg[a]	CH_2CHCl	8.7 ± 0.2	−6.3 ± 1.0	10.0 ± 0.1 (−80)
2	tg	CH_2CHCl	8.6 ± 0.6	−5.9 ± 2.0	9.8 ± 0.1 (−80)
3	tg	CH_2CHCl	8.1 ± 0.8	−9.9 ± 5.0	10.0 ± 0.1 (−80)
4	tg	CH_2CHCl	7.9 ± 0.9	−10.0 ± 5.0	9.8 ± 0.1 (−80)
5	tg	CH_2CHCl	8.7 ± 0.5	−6.4 ± 3.0	10.0 ± 0.1 (−80)
6	tg	CH_2CHCl	7.8 ± 0.8	−10.0 ± 4.0	9.7 ± 0.1 (−80)
7	tg	$CBrF_3$	8.9 ± 0.3	−4.6 ± 2.0	9.8 ± 0.1 (−80)
8	tg	$CBrF_3$	8.2 ± 0.5	−4.0 ± 2.0	8.9 ± 0.1 (−80)
9	tg	CH_2CHCl	8.5 ± 0.6	−7.8 ± 4.0	10.0 ± 0.1 (−80)
10	tg	CH_2CHCl	8.6 ± 0.8	−1.7 ± 4.0	8.9 ± 0.1 (−80)
11	t-C_4H_9 rot[b]	CH_2CHCl	8.0 ± 0.5	1.0 ± 2.0	7.8 ± 0.1 (−80)
12[c]	t-C_4H_9 rot	CH_2CHCl			9.3 ± 0.4 (−100)

[a] Conversion of trans to one gauche rotamer. [b] *tert*-Butyl rotation. [c] Reference 13.

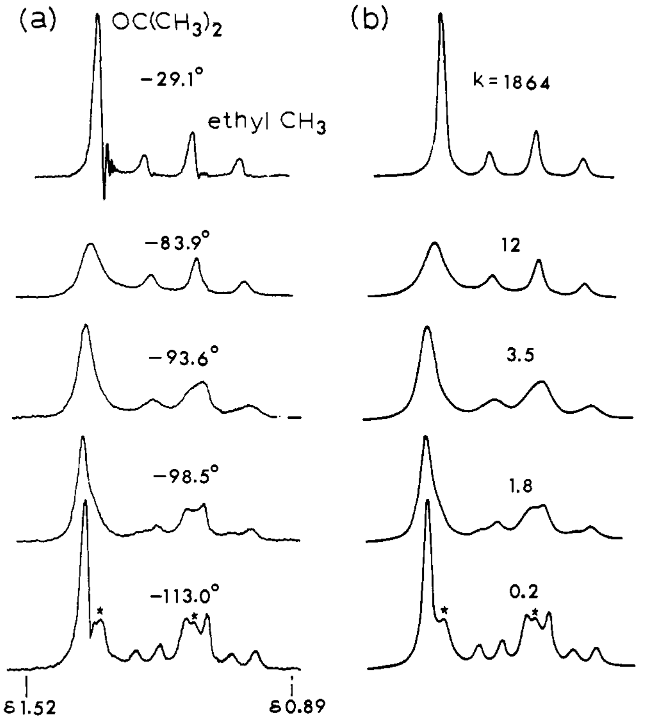


Figure 2. (a) Experimental ^{1}H DNMR spectra (60 MHz) of the $OC(CH_3)_2$ and ethyl CH_3 resonances of 2-bromo-3-ethoxy-2,3-dimethylbutane (**3**; 5% v/v in CH_2CHCl) at various temperatures. The two resonances at −113 °C marked with an asterisk are the two $OC(CH_3)_2$ singlets of the gauche conformer. (b) Theoretical ^{1}H DNMR spectra calculated as a function of the rate of trans/gauche equilibration assuming *no* gauche to gauche interconversion (k = first-order rate constant for the trans to gauche process).

Listed in Table III are the activation parameters for conversion of the trans rotamer to *one* gauche form in compounds **1–10** as well as activation parameters for *tert*-butyl rotation in other compounds of interest in this report.

Examination of the ^{1}H DNMR spectrum of 2-chloro-3-methoxy-2,3-dimethylbutane (**2**; 3% v/v in CH_2CHCl) showed a singlet $OC(CH_3)_2$ resonance (δ 1.26) which broadens at lower temperatures and is separated at −128 °C into a large singlet (δ 1.32) and two smaller singlets of equal area at δ 1.30 (overlaps large singlet) and 1.13. The ratio of the total area under the two small singlets to that under the large singlet is 45:55 at −128 °C. The OCH_3 resonance (δ 3.23 at −46 °C) is also separated at −128 °C into two singlets at δ 3.23 and 3.21 with a respective area ratio of 45:55. Such spectral behavior can of course be interpreted in terms of slowing rotation about the C(2)–C(3) bond of **2** (eq 1, R = CH_3; X = Cl) and the presence of gauche (δ 1.30, 1.13) and trans (δ 1.32) rotamers. Complete ^{1}H DNMR line shape analyses in the region of exchange broadening required an effective rate constant of zero for the gauche to gauche process and variable rates of gauche to trans equilibration. This is of course completely consistent with the dynamical model employed to simulate theoretical DNMR spectra for **1**. Pertinent thermodynamic, chemical shift, and activation parameters for **2** in CH_2CHCl and $CBrF_3$ are compiled in Tables I, II, and III.

Examination of the ^{1}H DNMR spectrum of 2-bromo-3-ethoxy-2,3-dimethylbutane (**3**; 5% v/v in CH_2CHCl) at −29.1 °C shows a singlet $OC(CH_3)_2$ signal (δ 1.35) and an ethyl CH_3 triplet (δ 1.10; ${}^3J$ = 7.0 Hz) as illustrated in Figure 2. At lower temperatures (Figure 2), the $OC(CH_3)_2$ resonance separates into a large singlet (δ 1.39) and two smaller singlets of equal area at δ 1.35 and 1.12 as determined from a complete H DNMR line shape analysis to be described below. The two small singlets are labeled with an asterisk on the experimental and theoretical spectra at −113 °C in Figure 2. The ethyl CH_3 signal is separated at −113 °C into two overlapping triplets at δ 1.13 (${}^3J$ = 7.0 Hz) and 1.08 (${}^3J$ = 7.0 Hz). Such spectral behavior is of course consistent with slowing C(2)–C(3) rotation (eq 1, R = CH_2CH_3; X = Br) with the two smaller $OC(CH_3)_2$ resonances (δ 1.35, 1.12) and the ethyl CH_3 triplet at δ 1.13 assigned to the gauche rotamer (eq 1). The trans form (eq 1) gives one large singlet resonance for the $OC(CH_3)_2$ group (δ 1.39) and one ethyl CH_3 triplet (δ 1.08). A complete ^{1}H DNMR line shape analysis verified this interpretation. In Figure 3a, a calculated spectrum of the $OC(CH_3)_2$ and ethyl CH_3 resonances of the trans rotamer *only* is presented with the corresponding gauche spectrum (asterisks on $OC(CH_3)_2$ singlets) in Figure 3b. The two spectra in Figures 3a and 3b are added to give the composite spectrum in Figure 3c which incorporates a gauche:trans ratio of 40:60 and which gives an excellent fit to the experimental spectrum at −113 °C (Figure 2). Again, the kinetic model used to generate theoretical DNMR spectra in the region of exchange broadening (Figure 2) incorporated an effective rate constant of zero for the gauche to gauche process and variable rates of gauche to trans equilibration. The computer program "ADNFW" used to generate the theoretical DNMR spectra in Figure 2 was developed in our laboratory by an appropriate modification of the "spectral vector" output of our locally modified program DNMR3.[15] ADNFW allows the calculation of DNMR spectra resulting from the superposition of separate and distinct spin systems all of which may be subject to the same or different dynamical exchange processes. Activation parameters for the trans to gauche process are compiled in Table III. Due to severe peak overlap (Figure 2) and the presence of a small amount (~2%)

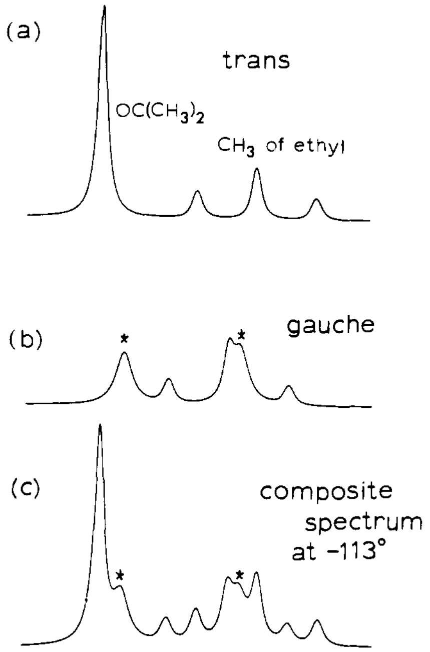


Figure 3. (a) Calculated ^{1}H DNMR spectrum of $OC(CH_3)_2$ and ethyl CH_3 resonances of trans rotamer *only* of 2-bromo-3-ethoxy-2,3-dimethylbutane. (b) Gauche rotamer only ($OC(CH_3)_2$ singlets indicated by an asterisk). (c) Composite spectrum with 60% trans and 40% gauche under conditions of static C(2)–C(3) rotation.

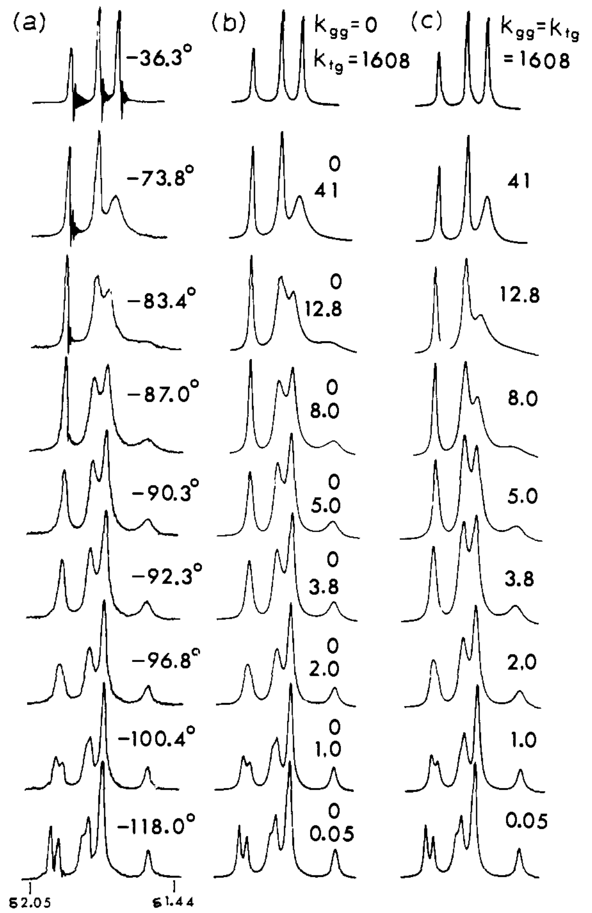


Figure 4. (a) The complete ^{1}H DNMR spectra (60 MHz) of 2-bromo-3-acetoxy-2,3-dimethylbutane (**5**; 5% v/v in CH_2CHCl) at various temperatures. (b) Theoretical ^{1}H DNMR spectra calculated as a function of the rate of trans/gauche equilibration assuming *no* gauche to gauche conversion (k_{gg} and k_{tg} (s^{-1}) are defined in the caption to Figure 1b). (c) Theoretical ^{1}H DNMR spectra calculated using *equal* rate constants for the trans to gauche and gauche to gauche processes.

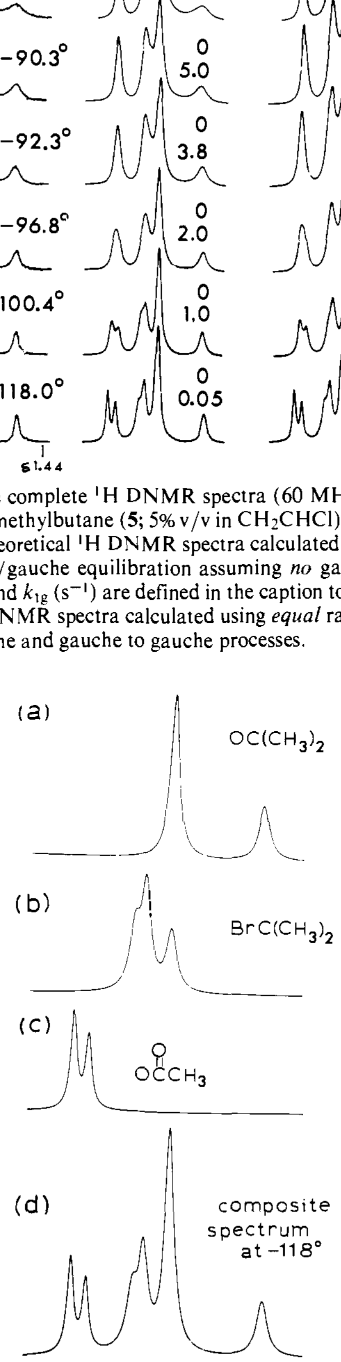
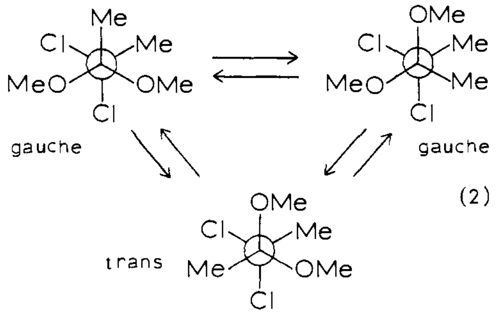


Figure 5. A dissection of the ^{1}H DNMR spectrum of 2-bromo-3-acetoxy-2,3-dimethylbutane (**5**; 5% v/v in CH_2CHCl) under conditions of slow C(2)–C(3) rotation: (a) the $OC(CH_3)_2$ group, (b) the $BrC(CH_3)_2$ group, (c) the O_2CCH_3 group, and (d) composite spectrum of (a), (b), and (c).

of a persistent impurity, we could not determine gauche:trans ratios with adequate precision to warrant calculation of $\Delta H°$ and $\Delta S°$ values. Therefore, the gauche: trans ratio in **3** at only one temperature is compiled in Table I. Similar behavior was observed for 2-chloro-3-ethoxy-2,3-dimethylbutane (**4**; 5% v/v in CH_2CHCl) and pertinent thermodynamic, DNMR, and activation parameters are compiled in Tables I, II, and III.

Examination of the ^{1}H DNMR spectrum of 2-bromo-3-acetoxy-2,3-dimethylbutane (**5**; 5% v/v in CH_2CHCl) at about -36 °C revealed three singlet resonances at δ 1.96 (3 H), 1.78 (6 H), and 1.68 (6 H) as illustrated in Figure 4. The singlet at δ 1.96 (3 H) can be assigned without ambiguity to the acetoxy methyl. By analogy with compounds **1–4**, the singlet at δ 1.68 is assigned to the $OC(CH_3)_2$ group and that at δ 1.78 to the $BrC(CH_3)_2$ group. Although these assignments have an arbitrary character, they are not critical to interpretation of changes in the DNMR spectra of **5** in terms of the gauche to trans equilibration discussed below. At lower temperatures (Figure 4), the O_2CCH_3 resonance is separated into two singlets of unequal area at -118 °C and the remainder of the spectrum undergoes dramatic and apparently complex changes. However, in light of the DNMR spectral behavior for compounds **1–4** and with the ability to superimpose separate DNMR spin systems using our computer program ADNEW, dissection of the gem-dimethyl DNMR spectra of **5** was possible. In Figure 5a–c, the *separate* ^{1}H DNMR spectra for the acetoxy and gem-dimethyl groups are illustrated under conditions of slow C(2)–C(3) rotation (eq 1, R = O═CCH$_3$; X = Br). In Figure 5a, the slow-exchange $OC(CH_3)_2$ resonance is composed of a large singlet (trans) and two small singlets of equal area (gauche) of which one is superimposed on the trans peak (Table II). A similar spectrum is dissected for the $BrC(CH_3)_2$ resonance (Figure 5b). In Figure 5c, the two O_2CCH_3 resonances are illustrated. The spectra in Figures 5a–c are then added to give the observed composite spectrum at -118 °C in Figure 5d. A correlation of peak areas at -118 °C for the $OC(CH_3)_2$ and $BrC(CH_3)_2$ resonances revealed the $O_2C(CH_3)$ peak at δ 1.98 to be due to the gauche rotamers and that at δ 1.94 due to the trans. Although apparently more complex, such DNMR spectral behavior is completely consistent with slowing gauche to trans equilibration (eq 1, $R = O{=}CCH_3$; $X = Br$) and the respective symmetries of gauche and trans conformers (eq 1). In Figure 4b, theoretical ^1H DNMR spectra are illustrated under conditions of fast, intermediate, and slow rates of C(2)–C(3) rotation using again a dynamical model incorporating an effective rate constant of zero for the gauche to gauche process and variable rates of gauche to trans equilibration. As can be seen in Figure 4b, the fits of theoretical to experimental DNMR spectra are excellent. The DNMR spectra of **5** in the intermediate exchange region are in fact very sensitive to the dynamical model employed. For example, in Figure 4c, theoretical DNMR spectra are illustrated in which the rate constants for the gauche to gauche and trans to gauche processes are *equal.* Although the fast and slow rotation spectra in Figure 4c are identical with Figure 4b as they must be, there are *significant* differences in the region of intermediate rates of rotation which show a poor fit of the spectra in Figure 4c to the experimental spectra. This dynamical behavior is consistent with compounds **1–4.** Similar behavior to **5** is observed in the ^1H DNMR spectra of 2-chloro-3-acetoxy-2,3-dimethylbutane (**6;** 5% v/v in CH_2CHCl) with pertinent data compiled in Tables I–III.

Examination of the ^1H DNMR spectrum of 2,2-dichloro-3,3-dimethoxybutane (**8;** 5% v/v in $CBrF_3$) at about −79 °C revealed three singlet resonances at δ 1.62 (3 H, $OCCH_3$), 2.09 (3 H, $ClCCH_3$), and 3.38 (6 H, OCH_3) consistent with rapid C(2)–C(3) rotation (eq 2). At −130 °C, the OCH_3 resonance is separated into a large singlet at δ 3.39 and a much smaller singlet at δ 3.32 while the $OCCH_3$ peak is separated into two singlets of unequal area at δ 1.73 and 1.46. The area under the smaller OCH_3 peak (δ 3.32) is *equal* to the area under the smaller $OCCH_3$ resonance (δ 1.46). The most reasonable interpretation of such spectral behavior is slowing C(2)–C(3) rotation (eq 2) on the DNMR time scale. The smaller OCH_3 resonance may be assigned to *one* of the nonequivalent OCH_3 groups of the gauche (eq 2) with the other OCH_3 peak exactly superimposed on the larger trans signal. This interpretation is consistent with the observation that the area under the smaller OCH_3 resonance is equal to that under the smaller $OCCH_3$ peak (δ 1.46) and allows assignment of the δ 1.46 resonance to the gauche form. Similar behavior is observed for compounds **7, 9,** and **10.** Pertinent data are compiled in Tables I–III.



(2)

At about −45 °C, the ^1H DNMR spectrum of 2,2-dimethyl-3,3-dimethoxybutane (**11;** 5% v/v in CH_2CHCl) is composed of three singlets at δ 3.24 (6 H, OCH_3), 1.25 (3 H, $OCCH_3$), and 0.96 (9 H, t-C_4H_9). The OCH_3 and $OCCH_3$ resonances remain singlets down to −130 °C while the t-C_4H_9 signal broadens and is separated at −130 °C into two singlets at δ 1.03 (3 H) and 0.92 (6 H). Such DNMR spectral changes for t-C_4H_9 are consistent with slowing t-C_4H_9 rotation on the DNMR time scale and the activation parameters derived from a complete DNMR line shape analysis are compiled in Table III.

Discussion

In considering the thermodynamic parameters associated with the rotamer preferences compiled in Table I, it must be kept in mind that these values refer to the *liquid* phase and probably do not accurately reflect gas phase conformational preferences. Indeed, the increased dielectric constant of the liquid phase usually leads to an increase in the concentration of more polar rotamers as compared to the gas phase due to increased dipolar solvation. Such differences in gas and liquid phase conformational preferences for rotamers of different dipole moment have been discussed in detail in quantitative terms by other authors.[9]

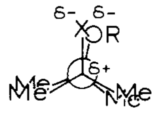
Thus, keeping in mind that we are dealing with liquid phase data, a perusal of the $\Delta H°$ values in Table I shows the gauche rotamer to be at *lower* enthalpy than the trans in every instance including two different solvents for **1** and **2.** In addition, the $\Delta S°$ values which have been corrected for the statistical preference for the gauche form (R ln 2) in Table I show the trans to be invariably higher in entropy than the gauche. The resultant $\Delta G°$ values which are all calculated at −110 °C then reveal a general preference *in terms of free energy* for the trans rotamer (Table I). *It is interesting to note that the $T\Delta S°$ term favoring the trans (Table I) is large enough to overcome the enthalpy ($\Delta H°$) preference for the gauche form at temperatures of interest in this report and the trans conformer prevails at equilibrium.*

The observation that the gauche rotamer is at lower enthalpy than the trans for compounds **1, 2, 5, 6,** and most likely **3** and **4** (Table I) is remarkable in light of the fact that this requires a crowding of all four rather large methyl groups on one side of the gauche conformer (eq 1). Increased dipolar solvation of the gauche form which would be expected to have a greater dipole moment than the trans must be invoked as an important factor.[9] Indeed, the solvent dependence of the $\Delta H°$ values for **1** and **2** in CH_2CHCl and $CBrF_3$ speaks for a preferential dipolar solvation effect. It would be expected that dipolar solvation of the gauche rotamer of **1** or **2** would be more efficient in the case of CH_2CHCl which has a dipole moment (μ) of 1.45 D than for $CBrF_3$ ($\mu = 0.65$ D). Stronger dipolar solvation of the gauche rotamer by CH_2CHCl could lead to an increased stabilization of the gauche rotamer relative to the trans in CH_2CHCl as opposed to $CBrF_3$. The $\Delta H°$ values compiled in Table I are consistent with this rationale. The higher entropy of the trans rotamer in *all* cases (Table I) is also consistent with less efficient dipolar solvation of the trans and *less solvent ordering* about the trans form as compared to the gauche. Another factor in the higher entropy of the trans could be a greater degree of rotational freedom for *individual* methyl groups as compared to the gauche in which all methyl groups are crowded together on one side of the rotamer (eq 1).

However, preferential dipolar solvation of the gauche rotamer cannot be the whole story when one compares the conformational preferences for **1** and **2** in the *same* solvent system. For example, **1** has a significantly greater preference in terms of enthalpy for the gauche rotamer than **2** in CH_2CHCl or $CBrF_3$ (Table I). Since the C–Cl and C–Br bond moments are very similar (~1.5 D),[17] it would be expected that the respective gauche and trans rotamers of **1** and **2** would have very similar net dipole moments and be subject to very similar dipolar solvation. If dipolar solvation were the *only* factor affecting conformational preference, **1** and **2** should have essentially identical conformational preferences. However, the increased amount of gauche rotamers in **1** as compared to **2** is consistent with other data for halogenated methylbutanes[12] and polyhalogenated ethanes[18] which indicate that bromine is indeed an effectively larger group than chlorine, i.e., bromine exerts greater van der Waals repulsive interactions than chlorine. In **1,** bromine has a choice of being gauche to two large methyl groups in the trans rotamer (eq 1) *or* gauche to only one large methyl group and one sterically smaller methoxyl functionality[4] in the gauche form. Thus, using steric arguments and considering previous data,[12,18] it would appear that the gauche form of **1** should have a lower enthalpy than the gauche form of **2** as compared to the respective trans geometries. This indeed appears to be the case (Table I) and speaks for the necessity to invoke dipolar solvation, van der Waals repulsions, and other possible yet-to-be-determined factors in rationalizing the conformational preferences in Table I.

The very similar $\Delta H°$ values (Table I) for **5** and **6** seem to suggest an increased importance for dipolar solvation as compared to **1** and **2**. For those compounds possessing four polar substituents (**7–10**), there is no general trend evident although one still observes the gauche rotamer to be at lower potential energy than the trans which is at higher entropy.

As discussed in the Results section, determination of the rates of C(2)–C(3) rotation in compounds **1–10** using complete ^{1}H DNMR line shape analyses *required* the use of a dynamical model which incorporates an effective rate constant of zero for the gauche to gauche rate process with the shape of the DNMR spectra dependent only on the gauche to trans to gauche itinerary (eq 1 and 2). The effect on the DNMR spectra is particularly dramatic in the case of compound **5** (Figure 4). In *all* cases (**1–10**), it is apparent that the gauche to gauche process possesses a barrier at least 0.5 kcal/mol higher than the trans to gauche conversion. In all cases (**1–10**), the transition state for the gauche to gauche interconversion involves maximum eclipsing of vicinal polar bonds and maximum eclipsing of vicinal methyl groups (**13;14**).



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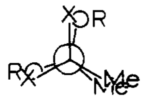

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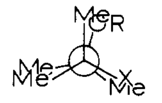
R = alkyl
X = halogen



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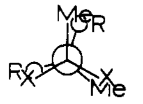

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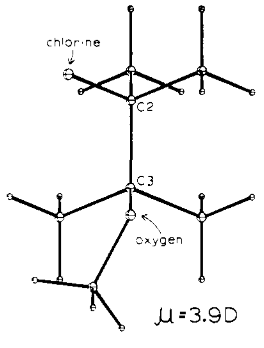
The higher barrier associated with the gauche to gauche process may be ascribed to significant electrostatic repulsions between the monopoles of eclipsed polar bonds and also to van der Waals repulsions between eclipsed methyl groups (**13;14**). The nature of the repulsions in the transition state for the trans to gauche process (**15;16**) is quite different. The number of eclipsings between two vicinal polar substituents *or* two vicinal methyl groups is minimized (**15;16**) with methyl eclipsing the sterically smaller alkoxyl group which leads apparently to a lowering of the barrier. The implication that a methyl/methoxyl vicinal eclipsed repulsion (e.g., see **15** and **16**) is less than a methyl/methyl repulsion is indeed supported by the barriers for *tert*-butyl rotation in **11** and **12** (Table III). The lower barrier in **11** as compared to **12** suggests that methoxyl is significantly less hindering to *tert*-butyl rotation than methyl.

The potential barriers ($\Delta H^{\ddagger}$) for the trans to gauche process in **1–10** are all comparable (Table III) revealing no dramatic substituent effects. One other undeniable trend is a consistently *negative* $\Delta S^{\ddagger}$ for the trans to gauche rate process (Table III). In proceeding from the trans rotamer to the gauche, the transition state should have a greater net dipole moment than the trans form and be subject to increased dipolar solvation. This increased dipolar solvation would of course lead to a decrease in entropy as observed. In addition, it is quite possible that rotation of individual methyl groups would be more restricted in the eclipsed transition state thus leading to a further decrease in entropy.

Theoretical calculations for 2-chloro-3-methoxy-2,3-dimethylbutane (**2**) using the INDO-A method parameterized for second-row elements[19] are consistent with the above rationale. Cartesian coordinates used in these calculations were obtained using the computer program COORD (time-sharing version).[20] The computations were performed using a modified version of CNINDO.[21] Standard values of bond lengths (C–C, 1.54 Å; C–H, 1.10 Å; C–O, 1.45 Å; C–Cl, 1.80 Å) were employed. The four bonds to carbon were arranged in perfect T_d symmetry in all cases and the COC bond angle was given a value of 110°. All individual methyl groups were kept perfectly staggered. *Except for rotation about the C(3)–O bond,* no geometry optimization was performed and the results described below employ essentially a rigid-rotor model. The geometry of minimum energy is indeed calculated to be the gauche form with a dihedral angle between the O–CH_3 and C(2)–C(3) bonds of 150° (**17**). The dipole moment of **17** is calculated (INDO-A) to be 3.9 D. Rotation about the C(3)–O bond to a dihedral angle of 180° increases the energy by 0.15 kcal/mol and gives a dipole moment of 4.4 D. Further rotation to a dihedral angle of 210° increases the energy above **17** by 0.22 kcal/mol and gives a dipole moment of 4.7 D. The trans geometry has an optimized O–CH_3/C(2)–C(3) dihedral angle of 150° (**18**) *or* 210° but is calculated to be 0.48 kcal/mol *less stable* than **17**. The dipole moment of **18** is calculated to be 2.2 D which is lower than **17** (3.9 D) consistent with our predictions. Although these theoretical calculations must be considered reflective of the conformational behavior of **2** in the *gas phase,* they are in remarkably good agreement with the $\Delta H°$ values in Table I. Since these theoretical calculations do not in any way account for solvation phenomena, the agreement may be fortuitous. However, they do agree very well with the data in the less polar $CBrF_3$ system in which solvation effects should be less than in CH_2CHCl (Table I).



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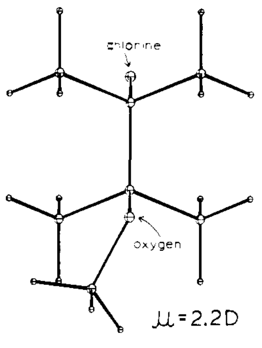

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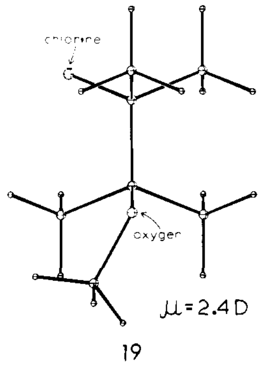
The energy of the eclipsed transition state for the gauche to trans process (e.g., **19**) is calculated to be 2.54 kcal/mol higher



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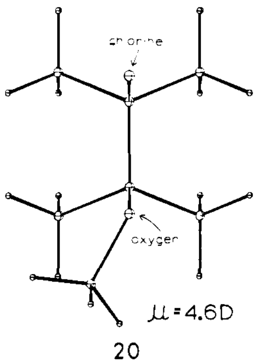

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in energy than the gauche (**17**) with a dipole moment of 2.4 D. Again the dihedral angle between C(2)–C(3) and the O–CH_3 bonds is optimized at 150° (**19**). A value of 210° increases the energy to 2.69 kcal/mol above **17** with a dipole moment of 3.5 D. The eclipsed transition state for the gauche to gauche process (**20**) is calculated to be 6.08 kcal/mol higher in energy than **17** and **20** is calculated to have a dipole moment of 4.6 D. Although the calculated barrier for the gauche to trans process (2.69 kcal/mol) does not agree quantitatively with experiment ($\Delta H^{\ddagger} \sim 9$ kcal/mol), the trend deduced from the DNMR studies indicating a *higher* barrier for the gauche to gauche process than for gauche to trans is clearly consistent with the theoretical calculations. Indeed, the fact that the experimental rotational barriers for the trans to gauche process in **8** and **10** are lower than **1, 2, 3,** and **4** allows one to deduce the following trend in vicinal eclipsed repulsions: $CH_3/CH_3 \sim OCH_3/Br > Cl/OCH_3$.

Experimental Section

The ^1H DNMR spectra were obtained using a Varian HR-60A NMR spectrometer equipped with a custom-built variable-temperature probe.[22]

The theoretical DNMR spectra were calculated using DEC PDP-10 and RCA Spectra 70/46 computers and plotted using a Calcomp plotter.

All DNMR samples were degassed and prepared about 1 h before recording spectra.

Compounds **1–10** were prepared by the method of Reed[23] and in every case gave satisfactory elemental analyses and NMR spectra (see Results section and Table II). Compound **11** was prepared using an acid-catalyzed addition of methanol to 3,3-dimethyl-2-butanone.

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